REMARKS

The claims pending in the above-identified application have been rejected for lack of enablement. These rejections are respectfully traversed for the reasons indicated below and reconsideration is requested.

The pending claims have been amended to be directed to a preferred embodiment of the invention. Applicants' amendment of certain rejected claims is not to be construed as an admission that the Examiner's rejections were proper. The Applicants continue to believe that the rejected claims are described in and enabled by the specification, and are patentable over any cited references. The indicated claims have been amended for the sole purpose of advancing the case to allowance. The Applicants reserve the right to file a continuing application to continue the prosecution of the rejected claims as originally filed.

Amendments to the Claims

The claims as amended are now directed to a preferred embodiment of the invention, treating cancer cells with an agent that binds to a MAP kinase. The agent is defined as comprising an amino acid sequence of the β integrin subunit that comprises a binding domain for a MAP kinase or a polypeptide moiety sufficiently homologous with the binding domain to bind to the MAP kinase. The MAP kinase is selected from a group consisting of members of the ERK and JNK MAP kinase families. These amendments are supported in the specification as filed at least at p. 24, lines 12-21; p. 26, lines 3-11; p. 12, lines 3-7 and lines 15-17; and p. 24, lines 5-11.

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Effective Priority Date

The Examiner pointed out that the certified copies of Australian priority applications PQ 1248 and PQ 8003 provided to the Patent Office by the International Bureau contained only the odd-numbered pages of the specifications. Please find enclosed replacement certified copies from the Australian Patent Office.

The Examiner has also asserted that the priority applications lack adequate written description support for the instant method claims, stating that they contemplate only the direct interaction of a MAP kinase with the cytoplasmic domain of $\alpha v\beta 6$, whereas the instant claims extend to the interaction between a MAP kinase and any integrin. Thus, the Examiner has for the purposes of the prior art search given the instant application an effective priority date of 28 June 2000. With respect, the Applicants draw the Examiner's attention to p. 3, lines 15-22, of priority application PQ 8003. In particular, this disclosure states that:

> Reference to an "integrin" molecule should be understood as a reference to any molecule the functional activity of which includes binding to matrix ligands and cytokines. Further, the integrin molecule of the present invention is one, the functional activity of which, either directly or indirectly exhibits a role in the growth of a cell. The integrins represent a distinct structural family of adhesion molecules. In a *preferred embodiment*, the integrin is $\alpha v\beta 6$ or its functional equivalent or derivative. To the extent that it is not specified, reference to an integrin, in general, or $\alpha v\beta 6$ should be understood to include reference to functional equivalents and derivatives thereof. [Emphasis added]

Accordingly, it is submitted that priority application PQ 8003 makes it clear that the scope of that application was not limited to consideration of the integrin $\alpha v\beta 6$. It is also submitted that

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priority application PQ 1248 was substantially in the same terms as the PCT application from which this US application is derived.

Rejection for Lack of Enablement

With regard to the rejection under 35 USC § 112, the Examiner has asserted that the claims contain subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

In particular, the Examiner has asserted it would be undue experimentation without any reasonable expectation of success to practice the claimed methods, which encompass any integrin or MAP kinase. The claims as amended now require that the MAP kinase be a member of the ERK and JNK MAP kinase families. As the Examiner has acknowledged, prior to the present invention, no MAP kinase or any other subunit form of MAP kinase had been shown to bind to an integrin. Integrins are transmembrane proteins located in the outer cell membrane. It was previously thought that MAP kinases played a role only in integrin mediated signaling *remotely* from the outer cell membrane via the conventional Ras/Raf/MEK/MAP kinase pathway. Accordingly, the finding that MAP kinases can bind directly to β integrin subunits *represents a major advance in the art*.

As shown in Example 10 of the present specification, the MAP kinase ERK 2 was found to bind not only to the β6 integrin subunit but to also the β3 and β5 integrin subunits. Inventor Michael Agrez has since shown that ERK2 can bind the β2 integrin subunit. The Examiner's attention is also drawn to Example 4 of the specification at p. 85, which teaches that the MAP kinase JNK-1 can bind to the β6 integrin subunit. Accordingly, the specification clearly shows that

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MAP kinase binding is not restricted to the β6 integrin subunit and further, that MAP kinase involvement is not limited to ERK2.

Since the Applicants have shown that MAP kinases can bind to multiple β integrin subunits, it is submitted that those skilled in the art would be able to readily practice the invention as claimed on the basis of the teachings and methodology provided by the specification. In particular, the Examiner's attention is drawn to Examples 3 and 4 at p. 82-85, which disclose an ELISA protocol for detecting MAP kinase-integrin binding. Attention is also drawn, for instance, to p. 46, line 10 to p. 47, line 15, directed to assay methodology for screening agents for their capacity to inhibit the MAP kinase-integrin binding interaction. Methodology for localizing and characterizing the binding domains of β integrin subunits for MAP kinases is also disclosed in the specification at, for instance, p. 43, line 8 to p. 44, line 11, and Examples 3 at p. 82-85. While relatively short peptides comprising the binding domain of a β integrin subunit can be used in MAP kinase-integrin binding assays as described above, the cytoplasmic tail domain of a β integrin subunit may also be used (e.g., see Example 4).

Moreover, having recognized that MAP kinases can bind to β integrin subunits, an observation entirely unknown prior to the present invention, the Applicants submit that they are entitled to broad protection, given the support provided by the body of the specification, the absence of prior art teaching that MAP kinases can bind directly to β integrin subunits, and the Applicants' finding that administration of an agent comprising a binding domain of an integrin for a MAP kinase or polypeptide with sufficient homology to the binding domain can inhibit the growth of cancer cells.

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The claims have also now been amended to require that the agent comprise an amino acid sequence of the β integrin subunit that comprises a binding domain for the MAP kinase, or a polypeptide moiety sufficiently homologous with the binding domain to bind to the MAP kinase. As taught in the specification at p. 24, lines 5-11, and p. 84, line 5 to p. 85, line 7, the binding domain of a β integrin subunit may comprise amino acids that do not participate in the MAP kinase-integrin binding interaction and may be deleted without affecting the binding activity of the remaining "core amino acid sequence." Indeed, Inventor Michael Agrez has found that this is the case for at least the binding domains of the β2, β3, β5 and β6 integrin subunits. Modifications to the amino acid sequence of a binding domain of a β integrin subunit or core amino acid sequence thereof may also be provided such that while the amino acid sequence is changed, the ability to bind to the MAP kinase is retained. As will be understood by the Examiner, the skilled practioner would be able to readily make conservative and other amino acid changes to a given polypeptide/peptide and yet retain the desired binding characteristics of the parent molecule. Support for the use of such polypeptide/peptides in methods of the invention is found throughout the body of the specification.

Thus, the Applicants submit that all claims in the application are in condition for allowance and such action is respectfully requested.

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The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

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